REMARKS

Claims 86-96, 101-112 and 116-123 are pending. Claims 91, 106, 112, 114, and 115 have been withdrawn by the Examiner. Withdrawn claims 114 and 115 have been canceled. Claims 86-96, 101-112 and 116-123 have been amended without prejudice or disclaimer. Support for the claim amendments can be found in the application as filed, for example, at paragraphs [0029], [0182], [0184], [0186], [0243]-[0244], and Example 3 of US 2004/0229250. No new matter has been added.

Applicants understand that upon allowance of a generic claim (e.g., claim 86 and/or claim 101), withdrawn claims that depend from or otherwise incorporate all the limitations of an allowable generic claim will be re-entered and considered in the present application.

Applicants thank the Examiner for withdrawing the previously-raised claim objections, and rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, First Paragraph, Written Description.

Information Disclosure Statement

Applicants thank the Examiner for considering all of the references listed in the Information Disclosure Statement filed on May 28, 2010. An Information Disclosure Statement is filed herewith. Applicants respectfully request that the Office consider the references cited in the Information Disclosure Statement, initial the Statement, and provide copies of the initialed Statement to Applicants.

35 U.S.C. § 112, Second Paragraph

Applicants thank the Examiner for withdrawing part of the previously-raised indefiniteness rejection of claims 86-90, 92-96, 101-105, 107-111, and 116-123.

Claims 86-90, 92-96, 101-105, 107-111, and 116-123. At pages 4-5, the Office alleges that claims 86-90, 92-96, 98, 101-105, 107-111, and 116-123 are indefinite in the recitation of "exogenous sulfatase" or "exogenous Formylglycine Generating Enzyme."

Solely to expedite prosecution, claims 86, 92-94, 101, 107-109, 117, 119, 121, and 123 have been amended and no longer recite the term "exogenous." Withdrawal of this rejection of claims 86-90, 92-96, 101-105, 107-111, and 116-123 is respectfully requested.

Claims 86-90, 92-96, 101-105, 107-111, and 116-123. At pages 6-7, the Office alleges that claims 86-90, 92-96, 98, 101-105, 107-111, and 116-123 are indefinite because the recitation

of "the gene encoding the endogenous sulfatase" or "the gene encoding the endogenous Formylglycine Generating Enzyme" lacks sufficient antecedent basis.

Solely to expedite prosecution, claims 86, 101, and their dependencies have been amended to recite "an endogenous nucleic acid ... wherein the endogenous nucleic acid encodes a sulfatase" or "an endogenous nucleic acid ... wherein the endogenous nucleic acid encodes a Formylglycine Generating Enzyme" instead of "an endogenous sulfatase" or "an endogenous Formylglycine Generating Enzyme," respectively. Applicants respectfully request that this rejection of claims 86-90, 92-96, 98, 101-105, 107-111, and 116-123 be withdrawn.

Claims 86-90, 92-96, 101-105, 107-111, and 116-123. At page 7, the Office alleges that claims 86-90, 92-96, 98, 101-105, 107-111, and 116-123 are indefinite in the recitation of "the gene encoding the endogenous ... comprises a heterologous promoter upstream of an endogenous sulfatase gene genomic locus."

Solely to expedite prosecution, claims 86 and 101 have been amended and no longer recite the term "upstream of an endogenous Formylglycine Generating Enzyme gene genomic locus." Withdrawal of this rejection of claims 86-90, 92-96, 101-105, 107-111, and 116-123 is respectfully requested.

35 U.S.C. § 112, First Paragraph, Enablement

Applicants thank the Examiner for stating at pages 8-9 that the application enables an isolated sulfatase-producing cell expressing a sulfatase polypeptide and expressing an FGE polypeptide comprising SEQ ID NO:2 or amino acids 34-274 of SEQ ID NO:2, wherein expression of FGE is achieved by: 1) transformation of a sulfatase-producing cell with an expression vector encoding an FGE polypeptide comprising SEQ ID NO:2 or amino acids 34-274 of SEQ ID NO:2, or 2) replacing the endogenous genomic FGE promoter with a heterologous promoter, wherein the FGE polypeptide modifies a catalytic cysteine to a formylglycine of the encoded sulfatase such that the ratio of active sulfatase to total sulfatase produced by the cell is increased up to 100% relative to a corresponding cell not expressing the FGE.

The Office at pages 8-13 alleges that claims 86-90, 92-96, 101-105, 107-111, 113, and 116-123 are not enabled. Specifically, the Office alleges:

> the term "exogenous" is commonly defined in this context as an object coming from outside of the system and is broadly and reasonably interpreted as encompassing a sulfatase and FGE that are produced *outside* of the cell. Yet the claims require that the exogenous sulfatase and FGE are encoded by heterologous DNA *introduced into the cell.* (Office Action at page 10)

Applicants do not acquiesce to the Office's understanding or definition of the term *exogenous*. As an initial matter, Applicants respectfully submit that when the terms in the specification are clear and unambiguous, which they are in this case, it is improper for the Examiner to rely on dictionary definitions or what the Examiner has "commonly defined in this context" (Office action, pages 6, 10, and 14). Moreover, Applicants respectfully submit that the Office's definition for *exogenous* is inconsistent with how it is and was understood by those skilled in the art (Office action, page 10). However, in the interest of expediting prosecution, and as discussed above, claims 86, 92-94, 101, 107-109, 117, 119, 121, and 123 have been amended and no longer recite the term "exogenous."

The Office also alleges:

> the specification fails to provide a working example of a transgenic human organism comprising a sulfatase-producing cell as encompassed by the claims. Further, the specification fails to provide any specific guidance for modifying a cell within a human organism to achieve overexpression of a sulfatase and an FGE. (Office Action at page 12)

Solely in the interest of expediting prosecution, claims 86-96, 101-112 and 116-123 have been amended to recite a "cultured" sulfatase-producing cell, thereby obviating this rejection.

Applicants submit that the subject matter of the amended claims is enabled and respectfully request that this rejection be withdrawn.

35 U.S.C. § 102/103

The Office maintains its rejection and alleges that claims 86-90, 93-96, 101-105, 108-111, 113, 116-119, and 122-123 are anticipated, or rendered obvious, by Rommerskirch et al. (*Proc. Natl. Acad. Sci. USA* 89:2561-2565 (1992); "Rommerskirch"), as evidenced by Dierks et al. (*Cell* 113:435-444 (2003); "Dierks"[1]) and Wraith et al. (*Human Genet.* 87:205-206 (1991); "Wraith"). The Office alleges that

> the phrase "exogenous" and "encoded by heterologous DNA introduced into the cell" with respect to the recited sulfatase and FGE, while limiting and defining the process by

[1] It is Applicants' understanding that "Dierks" is being cited merely as post-filing evidence. Therefore, this reference is not discussed in response to the rejection.

> which the sulfatase or FGE polypeptide is produced, does not structurally or functionally distinguish the recited sulfatase and FGE over the sulfatase and FGE of normal human fibroblasts of Rommerskirch. (Office Action at page 14)

Applicants respectfully disagree with the Office's position.

As an initial matter, Applicants note that the claims no longer recite "exogenous" and "encoded by heterologous DNA introduced into the cell" with respect to the sulfatase and FGE. Thus, the amended claims no longer include the alleged product-by-process limitations (see Office Action, page 14)

Rather, the pending claims in question require, *inter alia*, that the cultured sulfatase-producing cell comprises (a) an endogenous sulfatase nucleic acid operably linked to a heterologous promoter or a heterologous nucleic acid encoding a sulfatase, and (b) an endogenous FGE nucleic acid operably linked to a heterologous promoter or a heterologous nucleic acid encoding an FGE.

Applicants' claims are directed to a cultured cell. Therefore, the introduction of a heterologous promoter or a heterologous nucleic acid encoding a sulfatase or FGE to a host cell would result in a cultured cell that distinguishes it from a normal sulfatase-producing cell.

As acknowledged by the Office, Rommerskirch teaches that **normal** human fibroblasts have increased expression of a sulfatase relative to chromosome X-linked-ichthyosis fibroblasts. Nothing in Rommerskirch teaches or suggests a cell comprising an endogenous sulfatase nucleic acid operably linked to a heterologous promoter or a heterologous nucleic acid encoding a sulfatase. Further, Rommerskirch fails to teach a cell comprising an endogenous FGE nucleic acid operably linked to a heterologous promoter or a heterologous nucleic acid encoding an FGE. Thus, the cells recited in the pending claims are structurally different from Rommerskirch's normal fibroblasts.

Wraith fails to remedy these deficiencies.

Wraith describes the clinical phenotype of two patients with a complete deletion of the iduronate-2-sulphatase gene. Wraith does not teach or suggest a cell comprising an endogenous sulfatase nucleic acid operably linked to a heterologous promoter or a heterologous nucleic acid encoding a sulfatase. Nor does Wraith teach or suggest a cell comprising an endogenous FGE nucleic acid operably linked to a heterologous promoter or a heterologous nucleic acid encoding an FGE.

For at least these reasons, Applicants submit that claims 86-90, 93-96, 101-105, 108-111, and 113 are not anticipated, or rendered obvious, by Rommerskirch, as evidenced by Dierks and Wraith. Withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicants respectfully submit that all of the pending claims are in condition for allowance, which action is expeditiously requested. Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do Applicants concede that there are not other good reasons for patentability of the presented claims or other claims.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, please charge any deficiency to Deposit Account No. 50/2762.

Respectfully submitted,
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Docket No.: S2071-702810
Date: February 9, 2011